Imaging of renal hyperparathyroidism using SPECT/CT with low-dose localizing CT

by
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Declaration

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December 2013

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ABSTRACT

Background: Hybrid imaging using single photon emission computed tomography/low dose (x-ray) computed tomography (SPECT/LDCT) is of benefit in preoperative scintigraphy of primary hyperparathyroidism. The role of SPECT/LDCT in preoperative assessment of renal hyperparathyroidism has not yet been examined. The aim of the study was to determine whether SPECT/LDCT conferred any benefit over SPECT alone in terms of detection and/or localization of hyperfunctioning parathyroid tissue in this patient group.

Methods: A retrospective study of patients with renal hyperparathyroidism and positive planar and SPECT scintigraphy was undertaken. All patients underwent planar scintigraphy using ^{99m}Tc-pertechnetate immediately followed by ^{99m}Tc-sestamibi as well as SPECT/LDCT 60 min after sestamibi injection and a delayed static image to assess for differential washout at 2-3 hours. Planar subtraction images were generated. For each patient, two nuclear physicians reported on planar+ SPECT images followed by planar + SPECT/LDCT images (assisted by a radiologist). Confidence for the presence of hyperfunctioning parathyroid tissue as well as confidence of location was scored on a Likert-type scale. Interpretation of planar + SPECT was compared with interpretation of planar + SPECT/LDCT. The impact of LDCT on equivocal lesions and number of ectopic lesions detected was also assessed.

Results: Twenty patients (M:13; F:7) imaged between February 2008 and June 2011 were included [mean age: 40 years (24 – 55)]. Mean creatinine was 687 µmol/l (169-1213), mean corrected calcium: 2.55 mmol/l (1.95-3.33) and median PTH 167 pmol/l (2.4 - >201). Thirty-five lesions were detected on planar and SPECT and this was unchanged after assessment of the LDCT data. Confidence for the presence of parathyroid pathology changed in 5 patients (5 lesions) with the addition of LDCT. LDCT changed the mean confidence of parathyroid pathology from 3.17 to 3.29 (p=0.16). Addition of LDCT reduced the number of equivocal lesions from 18 (14 patients) to 14 (10 patients) (p=0.13). The addition of LDCT changed localization in 4 lesions (3 patients). Confidence in localization of pathology changed in 9 lesions (7 patients) and the mean localization confidence score was improved from 4.2 to 4.46 (p=0.002) with LDCT. The number of lesions classified as ectopic increased from 5 (on planar+SPECT) to 8 (with addition of LDCT) (p=0.25).

Conclusion: In renal hyperparathyroidism SPECT/LDCT altered localization of lesions detected on planar and SPECT alone and improved reader confidence of localization accuracy. SPECT/LDCT conferred no additional benefit over SPECT in terms of detection, confidence of parathyroid pathology or ability to distinguish equivocal from non-equivocal parathyroid lesions. The addition of LDCT did not detect significantly more ectopic lesions. Whereas the minor improvement in reader

confidence of localization (with addition of LDCT) was of questionable clinical significance, we speculate that the changed and presumably improved localization of lesions on SPECT/LDCT had potential clinical impact in a significant proportion of patients. On this basis we recommend the use of hybrid SPECT/LDCT in imaging of renal hyperparathyroidism when surgery is considered.

ABSTRAK

Agtergrond: *Hibriedbeelding met enkelfoton emissie rekenaartomografie / lae dosis rekenaartomografie (EFERT/LDRT) is voordelig in pre-operatiewe beelding van primêre hiperparatiroïedisme. Die rol van EFERT/RT in pre-operatiewe evaluering van renale hiperparatiroïedisme is nog nie ondersoek nie. Die doel van hierdie studie was om in hierdie pasiëntgroep te bepaal of EFERT/RT 'n voordeel bo EFERT alleen verleen.*

Metode: *'n Retrospektiewe studie van pasiënte met renale hiperparatiroïedisme en positiewe planare en EFERT flikkergrafie is onderneem. Na die toediening van ^{99m}Tc-pertegnetaat is planare beelding op alle pasiënte gedoen, onmiddellik gevolg deur ^{99m}Tc-sestamibi sowel as EFERT/RT beelding 60 min na sestamibi inspuiting en 'n laat statiese beeld vir differensiële uitwas op 2-3 uur. Planare subtraksiebeelde is verkry. Twee kerngeneeskundiges het die planare + EFERT beelde van elke pasiënt gerapporteer, waarna die planare + EFERT/RT beelde met die hulp van 'n radioloog gerapporteer is. Sekerheid oor die teenwoordigheid van hiperfunksionerende paratiroïedweefsel sowel as die sekerheid oor die lokalisering daarvan, is op 'n Likert-tipe skaal verkry. Interpretasie van planare + EFERT is vergelyk met die interpretasie van planare + EFERT/RT. Die impak van LDRT op twyfelagtige letsels en die aantal ektopiese letsels waargeneem, is ook bepaal.*

Resultate: *Twintig pasiënte (M:13; F:7) met beelding tussen Februarie 2008 en Junie 2011 is ingesluit [gemiddelde ouderdom: 40 jaar (24-55)] . Die gemiddelde kreatinien was 687 µmol/l (169-1213), gemiddelde gekorrigeerde kalsium 2.55 mmol/l (1.95-3.33) en mediaan PTH 167 pmol/l (2.4->201). Vyf en dertig letsels is op planare en EFERT beelde waargeneem en was onveranderd na assessering van die LDRT-data. Sekerheid oor die teenwoordigheid van paratiroïedpatologie het verander in 5 pasiënte (5 letsels) met die toevoeging van LDRT. LDRT het die gemiddelde sekerheid van paratiroïedpatologie van 3.17 tot 3.29 verander ($p = 0.16$). Toevoeging van LDRT het die aantal twyfelagtige letsels van 18 (14 pasiënte) tot 14 (10 pasiënte) verminder ($p = 0.13$). Die byvoeging van LDRT het die lokalisering in 4 letsels (3 pasiënte) verander. Sekerheid oor die lokalisering van patologie is in 9 letsels (7 pasiënte) verander en die gemiddelde lokalisering betroubaarheidswaarde is verbeter van 4.2 tot 4.46 ($p = 0.002$) met LDRT. Met die byvoeging van LDRT het die aantal letsels geklassifiseer as ektopies van 5 tot 8 ($p = 0.25$) toegeneem.*

Gevolgtrekking: *In renale hiperparatiroïedisme het EFERT/RT die lokalisering van letsels wat op planare + EFERT beelding alleen waargeneem is, verander en die leser se vertroue om akkuraat te lokaliseer verbeter. EFERT/LDRT het geen bykomende voordeel bo EFERT in terme van die opsporing, sekerheid van paratiroïedpatologie of onderskeidingsvermoë tussen twyfelagtige teenoor*

nie-twyfelagtige paratiroïedletsels verleen nie. Met die byvoeging van LDRT is nie beduidend meer ektopiese letsels gevind nie. Terwyl die geringe verbetering in die sekerheid van lokalisering (met die byvoeging van LDRT) van twyfelagtige kliniese betekenis was, spekuleer ons dat die verandering en vermoedelik verbeterde lokalisering van letsels op EFERT/LDRT 'n potensiële kliniese impak het in 'n beduidende aantal pasiënte. Die gebruik van EFERT/LDRT in die beelding van renale hiperparatiroïedisme wanneer chirurgie oorweeg word, word dus vir bogenoemde rede aanbeveel.

Table of Contents

LIST OF FIGURES

LIST OF TABLES

INTRODUCTION AND LITERATURE REVIEW

In contrast to *de novo* neoplasia or hyperplasia of one or more of the parathyroid glands in primary hyperparathyroidism, secondary hyperparathyroidism refers to parathyroid hyperplasia in reaction to a chronic hypocalcaemic condition (most commonly renal failure), while tertiary hyperparathyroidism occurs almost exclusively in the context of long-standing renal disease when hyperplastic parathyroid glands develop functional autonomy and are no longer suppressible by correction of hypocalcaemia. While the diagnosis of hyperparathyroidism is principally biochemical, parathyroid scintigraphy has an established role in the detection of hyperfunctioning parathyroid tissue when surgery is being considered.[1]

While preoperative scintigraphy may be routinely indicated in cases of primary hyperparathyroidism, in renal hyperparathyroidism preoperative scintigraphy is also performed. Scintigraphy's main role in the renal patient group has been for detection of residual or recurrent hyperfunctioning glands post-surgery.[1–9] Routine preoperative scintigraphy of secondary or tertiary hyperparathyroidism is also performed by some centres. This is done based on its potential to reduce operative time, perform less extensive dissection, and to detect supernumerary or ectopic glands and thereby reduce the rate of surgical failure.[5,10–14] In addition it is possible that scintigraphy may be useful to plan management (surgical or medical), and to identify parathyroid tissue that should be conserved. [15] Its role is however controversial, in part due to the widely varying sensitivity (34-94%) and poor localization reported by several studies.[5,6,10,11,16–29] It can also be argued that surgical intervention in these cases typically mandates bilateral exploration and that accurate localization is therefore not as important as in cases of primary hyperparathyroidism in which minimally-invasive surgery is sometimes performed.[5,30]

The role of single photon emission computed tomography (SPECT) and hybrid imaging using SPECT together with a low-dose x-ray computed tomography (SPECT/LDCT) has been well-established for primary hyperparathyroidism. SPECT improves sensitivity and localization[29,31–37] and while SPECT/LDCT has no incremental value in sensitivity over SPECT alone,[8,31] it has been shown to improve localization.[8,31,38–40] While SPECT has been shown to increase sensitivity in detecting lesions in secondary and tertiary hyperparathyroidism,[18,26,29,41] and the value of SPECT fused with diagnostic CT in renal hyperparathyroidism has been demonstrated,[42] the role of SPECT/LDCT in this specific group has not been examined.

AIM OF THE INVESTIGATION

Our goal in this study was to determine the incremental value, if any, of performing SPECT/LDCT compared to SPECT, in cases of renal hyperparathyroidism.

MATERIALS AND METHODS

Patient selection

The scintigraphic studies of all patients with renal hyperparathyroidism (confirmed by laboratory and clinical data) who were referred to our department between February 2008 and June 2011 for parathyroid scintigraphy were reviewed. SPECT/CT was performed in all cases. Three patients had repeat scans and in these cases, the study with the most recent correlating biochemical data was selected. Only patient scans with lesions visible on SPECT were included in our study group. The study was conducted in accordance with established ethical guidelines and was approved by the ethics committee of our institution (Ref # N11/06/197).

Measures of Renal Disease

Information regarding specific renal pathology, medical management of hyperparathyroidism, dialysis, and whether a renal transplant had been performed was obtained for all patients. These data were recorded using a standardized data sheet.

Biochemical and Pathological Markers

Most recent plasma levels of parathyroid hormone, urea, creatinine, corrected calcium and phosphate at time of the scan were obtained. Parathyroid hormone levels post-surgery (if performed) were also recorded. The pathology and location of resected glands and masses were obtained when available.

Image Acquisition

Both subtraction and dual-phase techniques were used in imaging. All patients underwent planar scintigraphy using ^{99m}Tc-pertechnetate (imaging 15 min after intravenous injection of 74-111 MBq) immediately followed by ^{99m}Tc-sestamibi (imaging 5 min after intravenous injection of 740 MBq), as well as SPECT/LDCT 60 min after sestamibi injection. Planar subtraction images were generated from the acquired sestamibi and pertechnetate planar images.

Planar images were obtained on an Elscint APEX SPX 4 or Elscint APEX SP 4 camera using a pinhole collimator with a hole size of 3mm and a zoom factor of 1.8. A 256 x 256 acquisition matrix was used. Two pertechnetate anterior planar images were obtained over the thyroid (with and without a marker over sternal notch) at a distance of 5cm from collimator to surface of neck, for 300 seconds each. Without allowing the patient to move, sestamibi was then injected via an existing intravenous line and 5 minutes later 5 consecutive planar images were obtained in the same way. A single anterior image was then obtained at a distance of 20 cm, for 120 seconds.

Sixty minutes after injection of sestamibi, the patient was moved to an Infinia Hawkeye (GE Medical Systems) for SPECT/CT imaging. A Low Energy High Resolution collimator was used with a zoom factor of 1. The SPECT was acquired using a 128 x 128 matrix. A step and shoot protocol of 30 seconds per step, and 3 degrees per step was used and a total of 60 views per camera head was performed, giving a total of 120 projections. Both planar and SPECT images were obtained in word acquisition mode.

Immediately after the SPECT, without moving the patient, a low-dose CT was acquired using 10 mm slices with a current of 2.5 mA and voltage of 140kV with a 256 x 256 matrix. The CT was acquired at 2 revolutions/min for a total imaging time of approximately 11 minutes.

Transverse SPECT images were reconstructed using an ordered subset expectation maximization (OSEM) algorithm with 4 iterations with 30 subsets, and incorporated collimator blurring correction. No post-processing filters or attenuation correction was used.

The CT was reconstructed using a Hann filter with a cut-off frequency of 1.

A delayed pinhole image (identical imaging parameters to early images) after approximately 2-3 hours was acquired in most patients to assess differential washout. Planar subtraction images were generated.

Image Interpretation

Two Nuclear Medicine Physicians who were blinded to the biochemical, surgical and pathological results of the patients, interpreted the scintigraphic studies by consensus by first reporting the planar

images together with SPECT, and then the planar images together with SPECT/LDCT. The latter study was read together with a radiologist.

Similar to a method used in a previous study,[38] the Nuclear Medicine Physicians and Radiologist reported on the presence of hyperfunctioning parathyroid tissue, and its location (eutopic: left/right; superior/inferior; ectopic: inferior, intrathyroidal, mediastinal) for both planar with SPECT and planar with SPECT/LDCT. In addition, readers scored the confidence of hyperfunctioning parathyroid tissue (1=negative, 2 = equivocal, 3=moderate, 4=high) and confidence of location of pathology (0 = no gland detected, 1=very low, 2=low, 3=equivocal, 4=moderate, 5=high).

Statistical Analysis

In those lesions that were visible on planar and SPECT, comparisons were made between SPECT alone and SPECT/LDCT in terms of confidence for the presence of parathyroid pathology and confidence of pathology localization. Statistical significance was tested using a least squares means analysis of mean confidence scores. Tests of the ability of SPECT/LDCT to reduce the number of equivocal lesions and to detect additional ectopic lesions were conducted using a McNemar test.

RESULTS

Demographics

Of the 37 scans of patient with secondary or tertiary hyperparathyroidism reviewed, 20 had identifiable lesions on SPECT and were included in our retrospective analysis. Thirteen male patients and 7 female patients were included with a mean age of 40 years (range: 24 – 55 years).

Pathology and management measures

Measures of renal pathology, biochemistry, management and surgical findings (where available) are summarized in *Table 1*. Since the upper detectable limit of PTH in our institution is 201 pmol/l, and 6 patients exceeded this level, an accurate mean and maximum for PTH could not be determined (a median was determined).

Of the 20 patients included in the study 5 underwent subsequent parathyroid surgery.

Imaging findings

The impact of LDCT on imaging findings is summarized in *Table 2*.

Detection

Thirty-five lesions (in 20 patients) were visible on planar and SPECT component of SPECT/LDCT. No additional lesions were detected with the addition of LDCT.

Interpreter confidence for parathyroid pathology changed in 5 lesions (5 patients) with the addition of LDCT. Confidence of pathology scores increased in 4 lesions (4 patients) and decreased in 1 lesion (1 patient). In the latter case, an equivocal focus on SPECT localized to what was interpreted as necrotic lymph node on LDCT (*Figure 1*.)

The use of hybrid imaging changed the mean confidence from 3.17 (for planar and SPECT) to 3.29 (for planar and SPECT/LDCT) which was not statistically significant (p=0.16) (*Figure 2*). The addition of LDCT reduced the number of lesions with equivocal scores for pathology (score 2 or 3)

from 18 (in 14 patients) to 14 (in 10 patients) although this did not reach statistical significance (p=0.13) (*Figure 3*).

Localization

Of the 35 lesions identified on planar images and SPECT, 30 were found to be eutopic (in 19 patients) and 5 were found to be ectopic (in 5 patients). Planar and SPECT/LDCT imaging localized 27 lesions as eutopic (in 18 patients) and 8 lesions as ectopic (in 7 patients). Although LDCT increased the number of ectopic lesions, this was not statistically significant (p=0.25) (*Figure 4*.)

With the addition of LDCT the localization of 4/35 lesions changed (in 3 patients): Two glands (in 1 patient) initially localized as left and right inferior (eutopic) were localized as left and right inferior intrathyroidal (ectopic). The location of an additional gland was reclassified from inferior (eutopic) to inferior-posterior (ectopic) due to the addition of LDCT (*Figure 5*). The location of a final focus changed from left anterior mediastinal (ectopic) to inferior to left thyroid lobe (ectopic) but the discrepancy in interpretation might not have occurred had there not been incorrect positioning of the sternal marker on static images.

Confidence of localization of pathology changed in 9 lesions (7 patients) with the addition of LDCT. Mean confidence was improved from 4.2 (for planar and SPECT) to 4.46 (for planar and SPECT/LDCT) which was statistically significant (p=0.002) (*Figure 6*).

Correlation with surgical findings

For those patients who underwent surgery and for whom surgical records were available (n=5), 9 lesions were detected on scintigraphy while 19 parathyroid glands were resected (identification rate 47%). Pathological analysis revealed all resected glands to represent parathyroid hyperplasia. Unfortunately operative notes did not accurately record their location. The mean mass of resected parathyroid glands was 0.91 g. PTH levels post-surgery were available in 4 patients and demonstrated normalization in 2, near-normalization in 1 and persistent elevation in 1.

DISCUSSION

In this study we found that the addition of LDCT had no impact on 1.) detection; 2.) confidence of parathyroid pathology; 3.) number of equivocal lesions or 4.) number of ectopic lesions detected but did have some impact on the localization of hyperplastic and/or autonomous parathyroid tissue in renal hyperparathyroidism.

Although sensitivity and specificity could not be quantified in our study (since not all patients underwent surgery), no additional lesions were detected on LDCT and therefore there was no impact on the sensitivity of the investigation. This is consistent with studies in primary hyperparathyroidism that contained small subgroups with secondary hyperparathyroidism, in which sensitivity of SPECT and SPECT/LDCT was reported as equal. A study by Serra et al. (2006) comparing SPECT and SPECT/LDCT in patients with primary (n=10) and secondary (n=6) hyperparathyroidism found no difference in sensitivity between the two modalities.[8] Similarly, a study by Öksüz et al. (2011) that examined patients with primary (n=56) and secondary (n=-4) hyperparathyroidism reported identical sensitivity of SPECT and SPECT/LDCT.[31]

In our study, the addition of LDCT in the imaging of renal hyperparathyroidism had minimal impact on interpretation of lesions already identified. LDCT reduced the confidence of parathyroid pathology in 1 lesion out of 35 (in a single patient) from an equivocal parathyroid lesion without LDCT to a probable necrotic lymph node with LDCT. If the LDCT interpretation was correct this would have resulted in a small improvement in specificity. A minimal impact on specificity by LDCT is consistent with the previous study by Lavely et al. (2007) in patients with primary hyperparathyroidism (n=110) that reported no significant difference in specificity when comparing SPECT and SPECT/LDCT techniques (both > 98%).[38] Another previous study (using diagnostic CT) by Wimmer et al. (2010) reported no significant difference in specificity for CT fused with SPECT (93%) compared to SPECT alone (90%) in patients with multiglandular disease (renal hyperparathyroidism n= 22; primary hyperparathyroidism n=6).[42]

In our study, LDCT did not significantly improve interpreter confidence for parathyroid pathology, or reduce the number of equivocal lesions. While a previous study by Lavely et al (2007) included confidence of pathology scores (including scores for equivocal lesions) when comparing lesions detected on SPECT to SPECT/LDCT, no analysis of LDCT impact on confidence of pathology *per se* or number of equivocal lesions was performed.[38]

The localization of 4 out of 35 lesions (in 3 out of 20 patients) in our study was changed by the addition of LDCT (in 3 lesions from eutopic to ectopic locations and in 1 lesion from ectopic to

another ectopic location). The impact of LDCT may however have been less in the one patient had a sternal marker not been incorrectly positioned on planar imaging. The number of lesions in which LDCT changed localization is less than that reported in the study by Serra et al. (2006) that compared SPECT and SPECT/LDCT in 10 patients with primary hyperparathyroidism and 6 patients with secondary hyperparathyroidism. In their study, in the former group LDCT changed the localization of 7/14 lesions (6 patients) and in the latter group LDCT changed localization in 7/9 lesions (5 patients).[8]

In our study, LDCT improved interpreter confidence of localization. While this was statistically significant, the increase from a moderate score of 4.2 to a moderate score of 4.46 was of questionable clinical significance. A previous study by Lavely et al (2007) which examined LDCT in primary hyperparathyroidism measured confidence of localization with LDCT compared to SPECT alone, but used the results to assign a binary value (positive/negative for *a priori* locations) to lesions detected and did not examine improvement in localization scores with the addition of LDCT *per se*.[38]

Unfortunately accuracy of localization could not be determined in our study since no correlation was performed with surgical findings; however it is reasonable to suppose that changes in localization with LDCT most likely represented improvements in accuracy by virtue of relation to anatomical landmarks. Accuracy of localization has previously been examined using surgical localization as a gold standard. There is evidence that SPECT fused with diagnostic CT is more accurate in localization of hyperfunctioning parathyroid lesions than SPECT alone in both primary[43,44] and renal[42] hyperparathyroidism. Improved localization accuracy has also been demonstrated using SPECT/LDCT when compared to SPECT alone. Using surgical correlation, the study by Serra et al. (2006) in patients with primary (n=10) and secondary (n=6) hyperparathyroidism reported accuracy of localization of SPECT in 61% of detected lesions vs. 100% with SPECT/LDCT.[8] In the study by Lavely et al. (2007) in patients with primary hyperparathyroidism (n=110), a confidence of localization score of 4 or 5 was interpreted as positive and lower scores as negative. Using location at surgery as their gold standard, they evaluated and compared the sensitivity of various combinations of early and delayed SPECT with and without LDCT as well as planar imaging. Techniques using SPECT/LDCT were quantitatively more accurate in localizing pathological glands than SPECT-only techniques.[38] A study by Pata et al. (2010) reported that SPECT/LDCT correctly localized adenomas in patients with primary hyperparathyroidism and nodular goitre (n=33) as determined by operative findings in 87.5% of cases compared to 55.6% with SPECT (p=0.0001).[39] Studies by Ruf et al. (2007) in patients with primary hyperparathyroidism[40] and Öksüz et al. (2011) in patients with primary (n=56) and secondary (n=4) hyperparathyroidism[31] have reported improved accuracy of localization with addition of LDCT on a qualitative basis.

Whether SPECT/LDCT is more accurate in localization of ectopic lesions in renal hyperparathyroidism could not be tested in our study since the number of ectopic lesions was too small. Future research to examine this might be worthwhile since studies by Ruf et al. (2007) and

Öksüz et al. (2011) in primary hyperparathyroidism have demonstrated that LDCT's increased accuracy in localization is most pronounced in ectopic lesions.[31,40]

In our study, addition of LDCT characterized more lesions as ectopic when compared to planar and SPECT imaging alone, although this did not reach statistical significance. This is potentially important since the prevalence of ectopic glands in renal hyperparathyroidism may be higher than previously recognized.[14] Lavely et al. (2007), in their study in primary hyperparathyroidism reported that SPECT/LDCT detected more inferior-posterior lesions than SPECT alone[38] although another study by Gayed et al. (2005) in primary hyperparathyroidism reported no change in the number of ectopic lesions detected.[45]

It should be noted that changes in localization (with LDCT) were determined with the benefit of a radiologist opinion. The impact of LDCT might be less without such assistance in a clinical setting.

Whether addition of LDCT has a clinical impact is uncertain and was not measured in this study. It may however be speculated that the addition of LDCT would have changed management in one patient by identifying potential additional pathology (possible necrotic lymph node), and in 3 patients by virtue of altered localization. Clinical impact of LDCT in hyperparathyroidism has not been extensively studied. Pata et al. (2010) compared two groups of patients with primary hyperparathyroidism and nodular goitre, one imaged with SPECT alone (n=18) and one with SPECT/LDCT (n=15). The mean operative time in the former group was 56 min and in the latter group 38 min (p=0.034).[39] Other authors have speculated that LDCT may be beneficial due to improved direction of the surgeon to ectopic sites, or by avoiding futile exploration for ectopic glands which are not present.[38,46] As mentioned, Lavely et al. (2007) noted that a major advantage of SPECT/LDCT was its ability to differentiate between inferior and inferior-posterior glands. They speculated that since surgery for inferior-posterior glands is frequently more complex, pre-operative knowledge of such lesions would facilitate exploration.[38] Finally, the reclassification of a gland from eutopic to ectopic (more difficult surgery) may influence the decision to perform surgery in a patient with high anaesthetic risk.

LIMITATIONS

The retrospective nature of the study meant that data were often incomplete and not standardized. A prospective study correlated with anatomical location at surgery as well as objective measures of clinical impact of LDCT would be of value.

In our study, SPECT/LDCT was performed 60 minutes after the sestamibi injection. There is evidence to suggest that earlier SPECT (15 – 30 min) has greater sensitivity in primary

hyperparathyroidism.[38,47] Washout of sestamibi prior to tomographic imaging may in part account for the reason that only 20 patients of the initial 37 had lesions identifiable on SPECT. It is possible that had our SPECT scans been conducted earlier post-injection, we would have detected more lesions to evaluate.

The major limitation in our study was the absence of a gold standard in the majority of patients. Of the 20 patients, only 5 had parathyroid surgery following scintigraphy and surgical notes in these cases were limited in detail with respect to localization thus limiting evaluation of accuracy of localization of the scintigraphy. While it was not possible to comment on whether the localization changes with LDCT represented improvements in localization, this is likely, given the additional anatomical information obtained with LDCT.

Since surgery was not performed in all patients that were scanned (and on none of the patients with negative scans), only a detection rate (in this group) could be determined.

CONCLUSION

In our study of patients with renal hyperparathyroidism SPECT/LDCT altered localization of lesions detected on planar and SPECT alone and improved reader confidence of localization accuracy. The clinical impact of altered localization was not studied. SPECT/LDCT conferred no additional benefit over SPECT in terms of detection, confidence of parathyroid pathology or ability to distinguish equivocal from non-equivocal parathyroid lesions. The addition of LDCT did not detect significantly more ectopic lesions. It is uncertain whether LDCT makes a greater contribution to localization and clinical outcome of ectopic lesions in renal hyperparathyroidism (as is suggested by literature in primary hyperparathyroidism) and further research is needed to determine this.

Whereas the minor improvement in reader confidence of localization (with addition of LDCT) was of questionable clinical significance, we speculate that the changed and presumably improved localization of lesions on SPECT/LDCT had potential clinical impact in a significant proportion of patients. On this basis we recommend the use of hybrid SPECT/LDCT in imaging of renal hyperparathyroidism when surgery is considered.

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TABLES

Table 1. Pathological and biochemistry results of study group

Pt	**Renal diagnosis**	**Creatinine (µmol/l)**[†]	**Corrected Calcium (mmol/l)** [††]	**PTH (pmol/l)**[‡]	**Prior management**	**Parathyroidectomy after scan**	**Mass of excised glands (g)**[*]	**Repeat PTH post-surgery (pmol/l)** [‡]
1	Mesangiocapillary GN	1210	2.42	>201	CS: Yes VDS: Yes Dialysis: PD	Yes	LI:1.22 RI:2.78 RS:0.16	>201
2	Mesangiocapillary GN	541	1.95	>201	CS: Yes VDS: ? Dialysis: PD	Yes	LI:0.375 LS:0.335 RI:0.36 RS:0.246	4.5
3	Chronic GN	611	2.61	27.1	CS: Yes VDS: Yes Dialysis: HD	No		
4	ADPKD	302	2.24	148.4	CS: No	No		

					VDS: No Dialysis: No			
5	Chronic GN	1213	2.24	>201	CS: Yes VDS: Yes Dialysis: HD	Yes	LI:2.27 LS:0.1 RI:0.59 RS:0.21	2.7
6	Malignant Hypertension	691	2.35	178.6	CS: Yes VDS: Yes Dialysis: PD	?		
7	Chronic GN	765	2.07	145.1	CS: Yes VDS: No Dialysis: HD	No		
8	?	598	2.63	84.5	CS: ? VDS: ? Dialysis: ?	?		
9	Focal segmental GN	?	2.26	153.2	CS: Yes VDS: Yes Dialysis: HD	No		
10	Malignant Hypertension	513	3.03	133	CS: Yes	No		

					VDS: No Dialysis: HD			
11	Chronic GN	993	3.01	170.9	CS: ? VDS: Yes Dialysis: HD	No		
12	Malignant Hypertension	670	2.66	414	CS: Yes VDS: Yes Dialysis: HD	No		
13	Chronic GN	1200	2.4	105.3	CS: Yes VDS: Yes Dialysis: HD	No		
14	Malignant Hypertension	490	2.21	162.8	CS: Yes VDS: Yes Dialysis: HD	No		
15	Chronic GN	411	2.93	>201	CS: Yes VDS: Yes Dialysis: HD	Yes	LI:3.62 LS:0.16 RI:0.92 RS:0.3	10.1
16	Reflux nephropathy	169	3.28	>201	CS: No	No		

					VDS: No Dialysis: HD			
17	Solitary ectopic kidney following nephrectomy for right dysplastic kidney	749	2.5	172.1	CS: Yes VDS: Yes Dialysis: HD	Yes	Mass of glands unrecorded LI,LS,RI: parathyroid hyperplasia LI(2): thyroid nodule	?
18	Solitary kidney; Reflux nephropathy	791	2.3	48.9	CS: Yes VDS: No Dialysis: HD	No		
19	Malignant Hypertension	226	3.33	2.4	CS: No VDS: No Dialysis: No	No		
20	Chronic GN	910	2.52	>201	CS: Yes VDS: Yes Dialysis: HD	No		
$\overline{x}$		**687**	**2.55**	**147**				

			(median)
Range	**169 – 1213**	**1.95 – 3.33**	**2.4 - >201**

PTH: Parathyroid Hormone, **GN**: glomerulonephropathy, **ADPKD**: Autosomal Dominant Polycystic Kidney Disease, **CS**: Calcium supplementation, **VDS**: Vitamin D supplementation, **HD**: Haemodialysis, **PD**: Peritoneal Dialysis, **LI**: Left inferior, **LS**: Left superior, **RI**: Right inferior, **RS**: Right superior, **?** Unknown

† Reference range: 60 – 120 µmol/l, †† Reference range: 2.05 – 2.56 mmol/l, ‡ Reference range: 1.2 – 8.5 pmol/l, * Normal: < 0.04 g

Table 2. Impact of LDCT on study interpretation:

Patient	**Gland**	**Planar + SPECT**			**Planar + SPECT/LDCT**		
		Pathology confidence score	**Location**	**Location confidence score**	**Pathology confidence score**	**Location**	**Location confidence score**
1	1	4	LI	4	~	~	5
	2	2	E: midline inf	4	4	~	5
2	1	2	LS	4	~	~	~
3	1	2	LI	4	~	~	~
4	1	2	RI	4	~	~	~
	2	4	E: LAM	4	~	E:inf to L	5
5	1	4	LI	4	~	~	~

6	1	3	LS	4	~	~	~
	2	4	LI	4	~	~	~
	3	4	RS	4	~	~	5
7	1	2	LI	4	~	~	~
	2	2	RI	4	3	~	5
8	1	4	RI	5	~	~	~
9	1	2	LS	4	~	~	~
	2	3	LI	4	~	~	~
10	1	4	LS	5	~	~	~
	2	4	LI	4	~	~	~
11	1	4	E: LIP	5	~	~	~
	2	3	RI	5	4	~	~
12	2	4	RS	4	~	~	~
13	2	3	LI	4	~	~	~
14	1	4	LI	5	~	~	~
	2	4	RI	5	~	~	~
15	1	4	LI	4	~	E: LIIT	5
	2	4	RI	4	~	E: RIIT	5
16	1	4	LI	5	~	E: LIP	~
	2	3	RI	4	~	~	~
17	1	4	LS	4	~	~	~
	2	3	RI	4	4	~	5
	3	4	E: inf to L	4	~	~	~

18	1	2	LS	4	~	~	~
	2	2	LI	4	~	~	~
19	1	2	E: thoracic inlet R	4	1 ⫻	~	5
20	2	3	LI	4	~	~	~
	3	2	RS	4	~	~	~
Mean		**3.17**		**4.2**	**3.28**		**4.46**

LI: Left inferior, **RI**: Right inferior, **LS**: Left superior, **RS**: Right superior, **E**: Ectopic, **LIP**: Left inferior-posterior, **LIIT**: Left inferior intrathyroidal, **RIIT**: Right inferior intrathyroidal, **inf to L**: inferior to left thyroid lobe, **inf to R**: inferior to right thyroid lobe, **midline inf**: inferior to thyroid in the midline, **LAM**: left anterior mediastinum, **thoracic inlet R**: thoracic inlet right

~ Unchanged

⫻ LDCT demonstrated lesion most likely necrotic node and not parathyroid

ILLUSTRATIONS

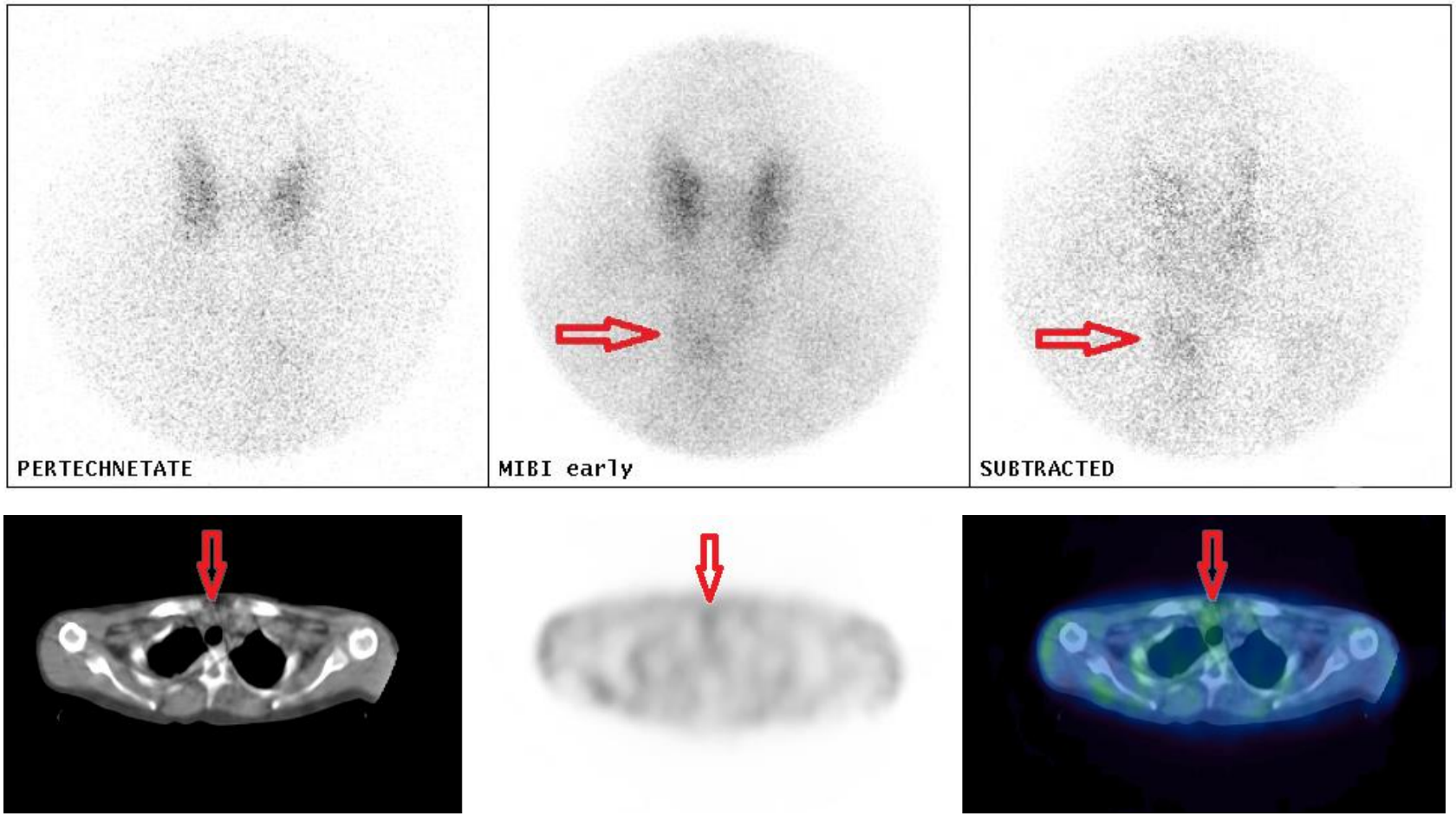

Figure 1. Planar and tomographic images of patient 35 demonstrating equivocal focus on planar imaging. On LDCT, this lesion was interpreted as most likely representing necrotic lymph node by the radiologist.

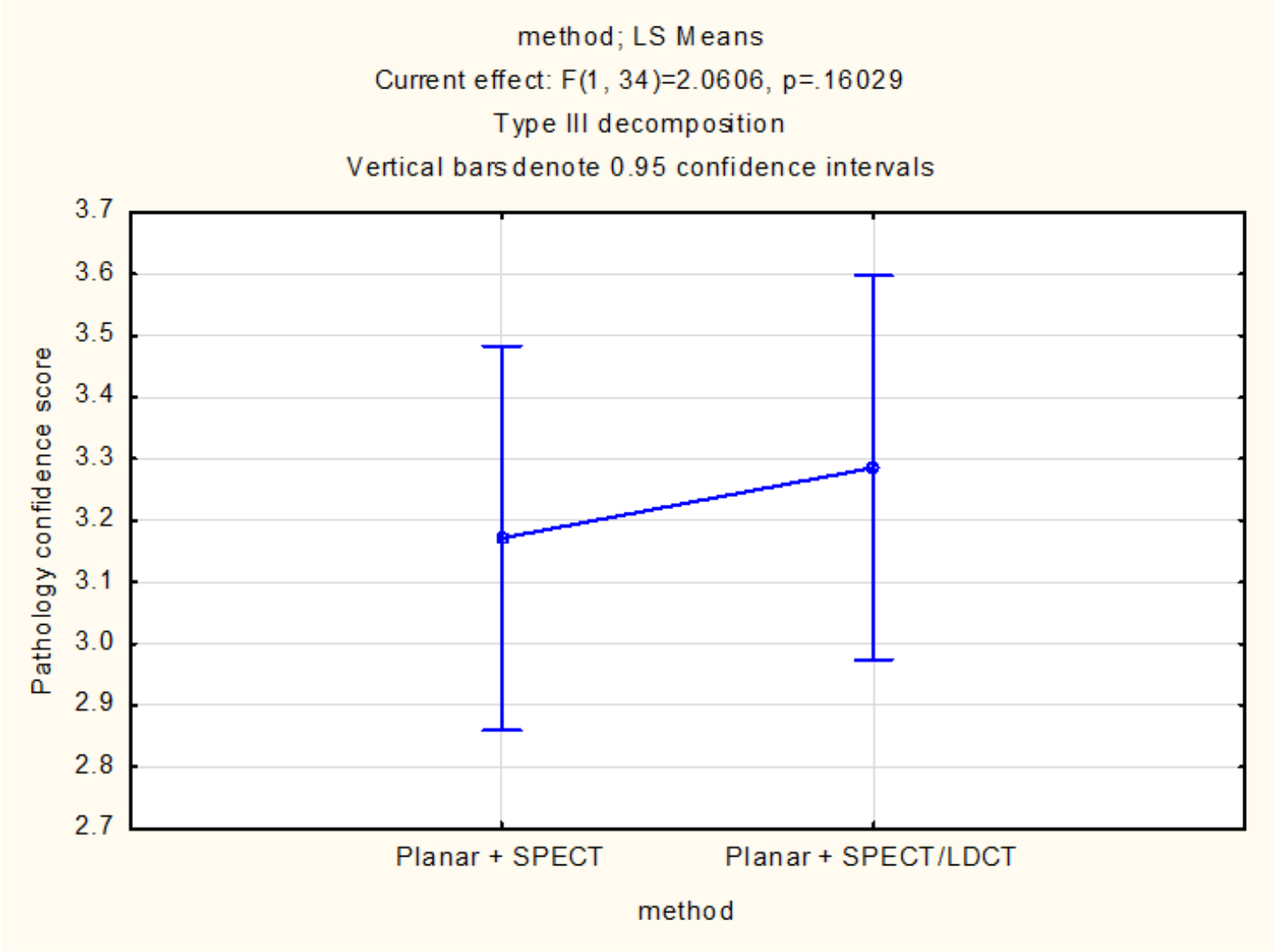

Figure 2. Impact of LDCT on pathology confidence score

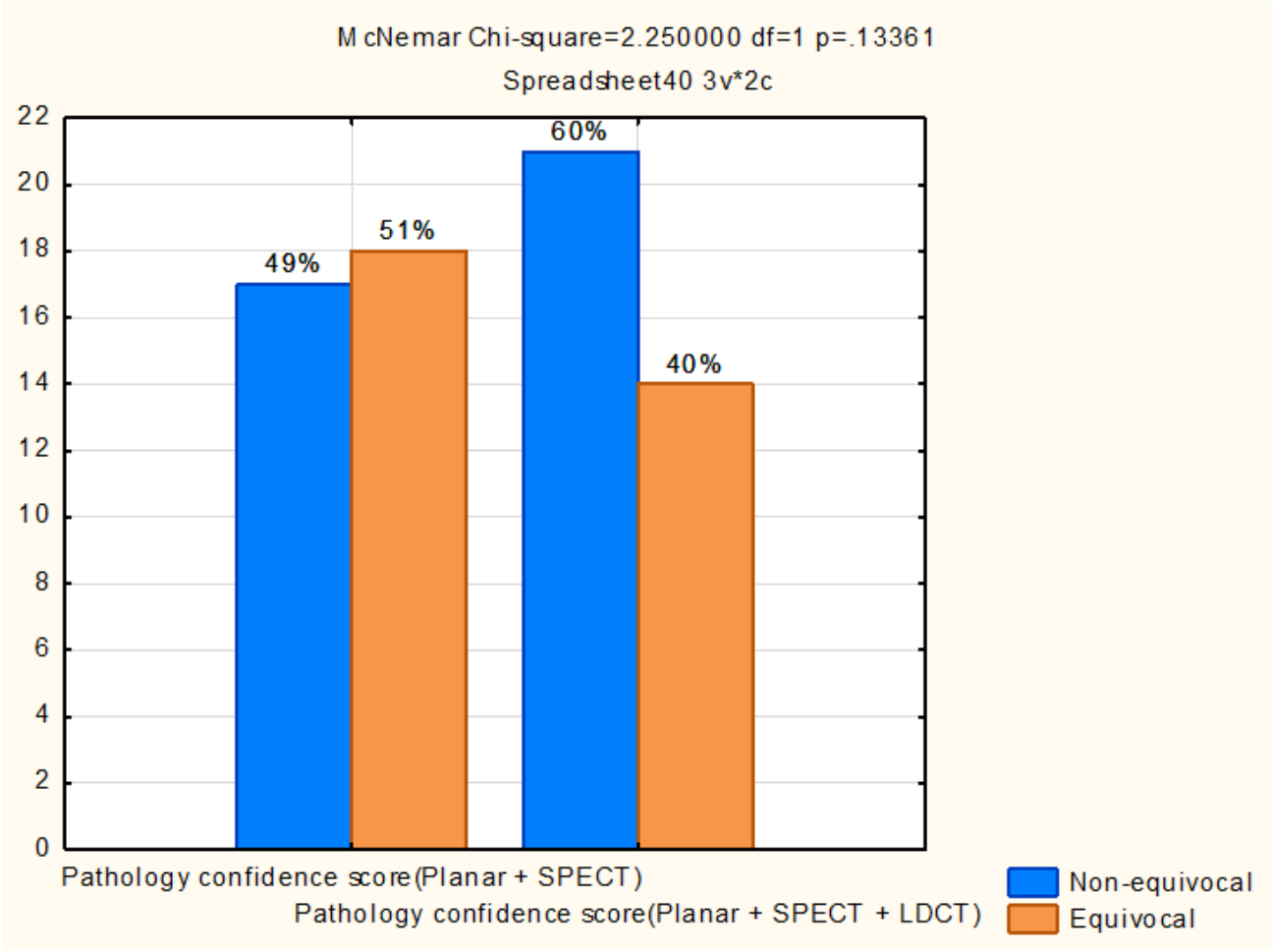

Figure 3. Impact of LDCT on proportion of equivocal lesions

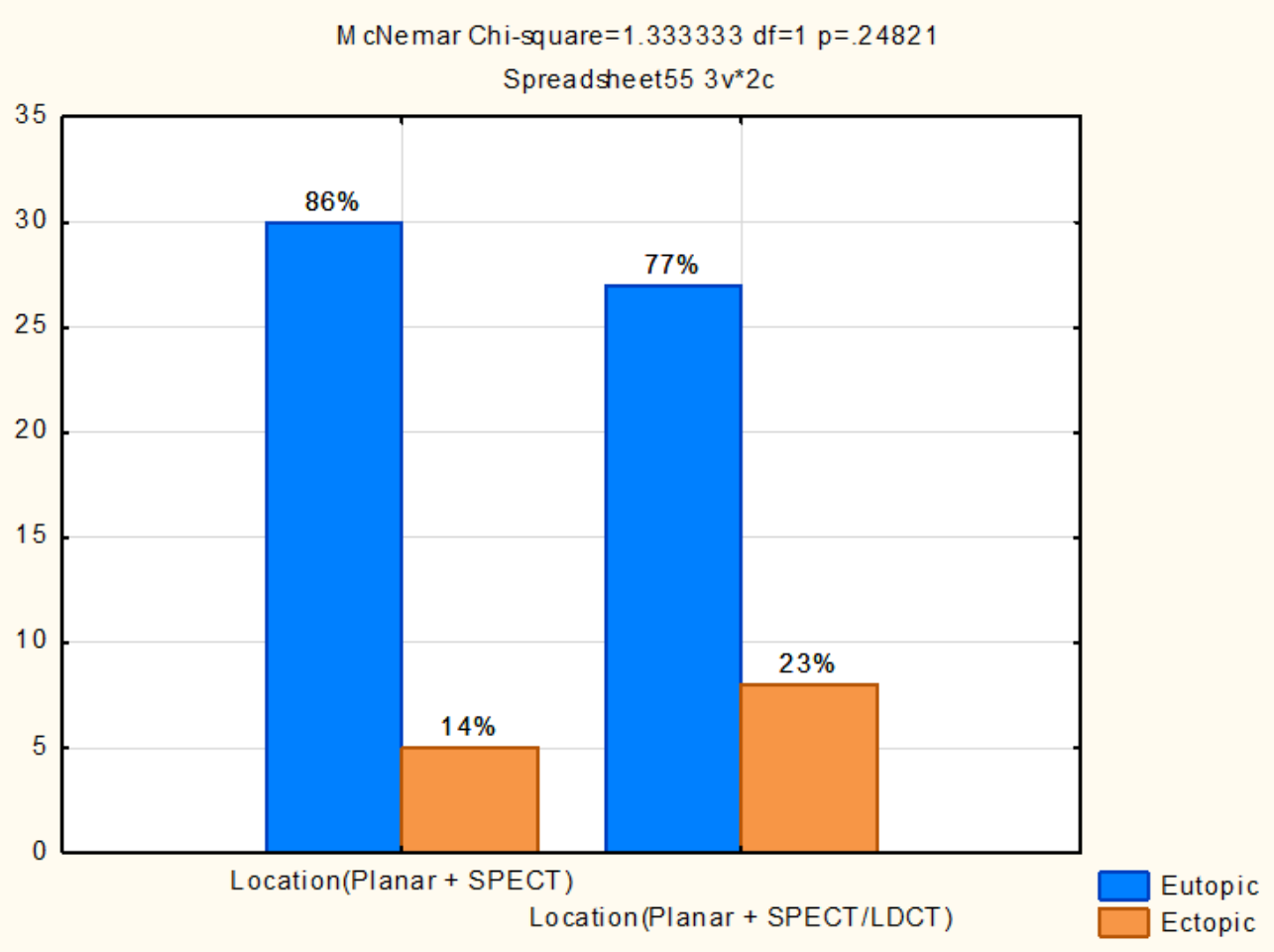

Figure 4. Impact of LDCT on proportion of ectopic lesions

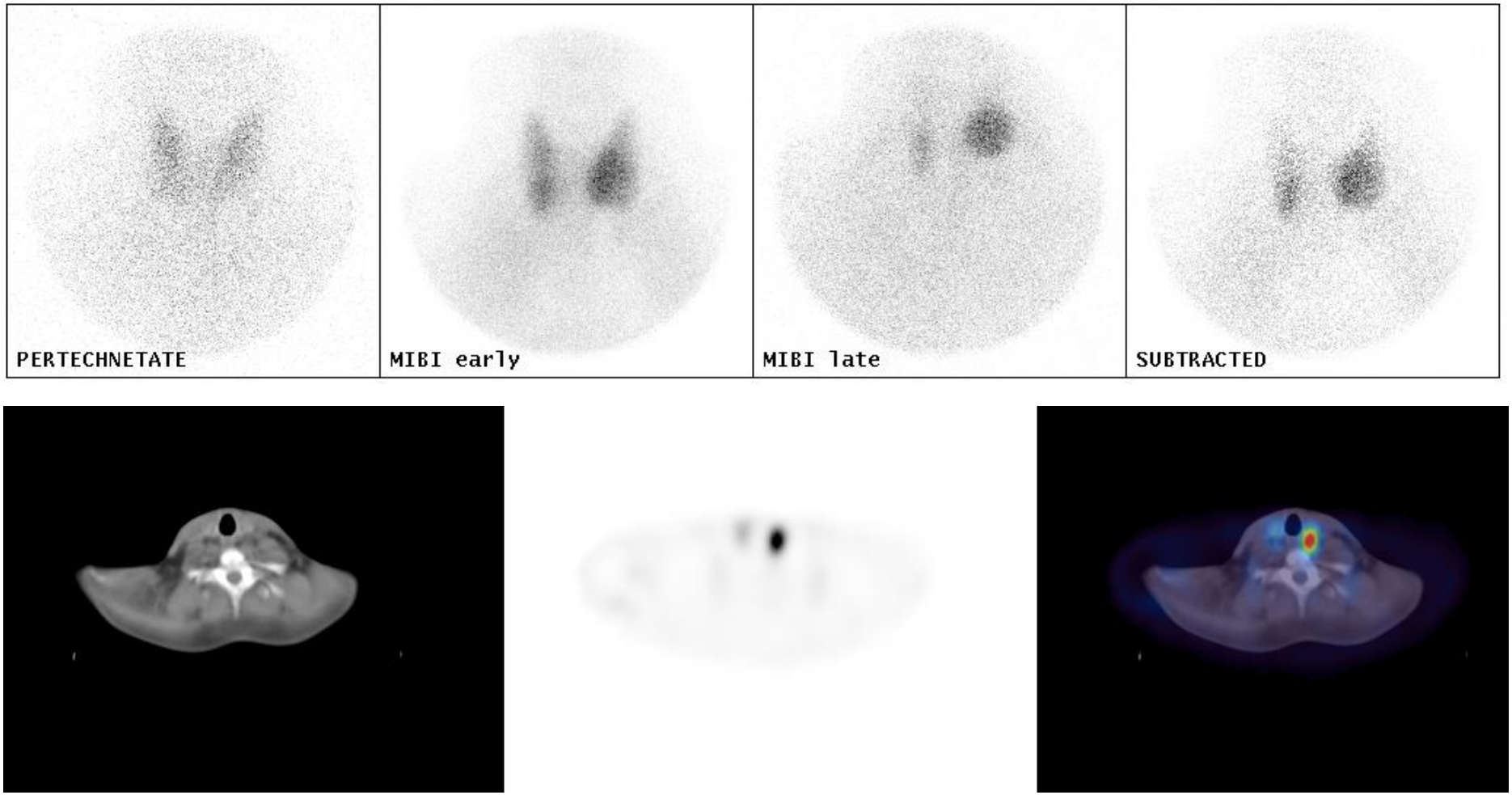

Figure 5. Planar and tomographic images of patient 29. Localization of the left focus was initially recorded as left inferior (eutopic) on interpretation of planar and SPECT data. Addition of LDCT altered localization to left inferior-posterior.

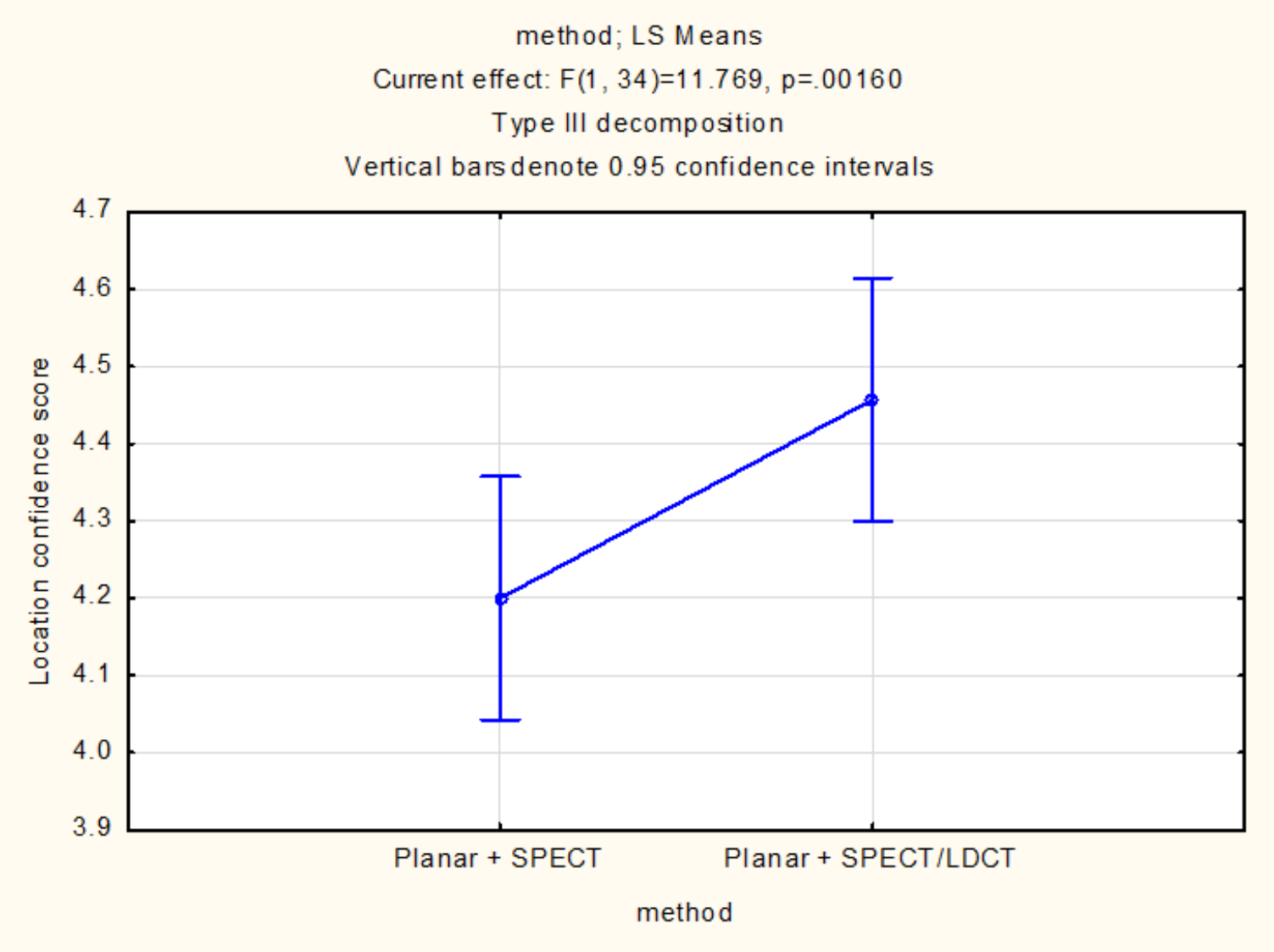

Figure 6. Impact of SPECT/LDCT on localization confidence score